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EXAMINER
ROONEY, NORA MAUREEN

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/027,625
Filing Date: December 29, 2000
Appellant(s): Stumvoll, Sabine
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Holly D. Kozlowski
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 05/27/2009 appealing from the Office action mailed 11/28/2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

European Patent Application Publication 0 707 065 A2

Duro et al. 'cDNA cloning, sequence analysis and allergological characterization of Par j 2.0101, a new major allergen of the *Parietaria judaica* pollen.' FEBS Letters. 399:295-298, 1996.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

A. Claims 30-32 and 34-35 stand rejected under 35 U.S.C. 102(b) as being anticipated by European Patent Application Publication 0 707 065 A2.

European Patent Application Publication 0 707 065 A2 teaches a method for serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria* allergic, comprising selecting an individual known to be weed pollen allergic, wherein it is not known if the individual is *Parietaria* allergic; selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity; contacting serum from an the selected individual with the pure allergen component, wherein the pure allergen component is pure Par j 1 allergen component; determining the presence of IgE binding to said pure Par j 1 component; and identifying the individual as *Parietaria* allergic if the contacted serum contains IgE binding to said pure allergen component; wherein the pure allergen component is recombinant Par j 1; and further comprising selecting an allergy treatment involving extract, proteins or peptides derived from a *Parietaria* species for an individual identified as *Parietaria* allergic. (In particular, page 4, lines 41-47, page 5, lines 31-32, page 7, lines 5-31, page 8, lines 49-59, Figure 8, abstract).

It is noted that the recitation of "an individual known to be weed pollen allergic" is anticipated by the fact that the diagnostic method of European Patent Application Publication 0 707 065 A2 is directed toward diagnostic procedures for all individuals, which includes those known to be weed pollen allergic. A diagnostic procedure which identifies *Parietaria* allergic individuals from all individuals will inherently identify *Parietaria* allergic individuals from weed pollen allergic individuals.

The reference teachings anticipate the claimed invention.

B. Claims 30, 33-34 and 36 stand rejected under 35 U.S.C. 103(a) as being unpatentable over European Patent Application Publication 0 707 065 A2 in view of Duro et al.

European Patent Application Publication 0 707 065 A2 teaches a method for serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria* allergic, comprising selecting an individual known to be weed pollen allergic, wherein it is not known if the individual is *Parietaria* allergic; selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity; contacting serum from an the selected individual with the pure allergen component, wherein the pure allergen component is pure Par j 1 allergen component; determining the presence of IgE binding to said pure Par j 1 component; and identifying the individual as *Parietaria* allergic if the contacted serum contains IgE binding to said pure allergen component; wherein the pure allergen component is recombinant Par j 1. (In particular, page 4, lines 41-47, page 5, lines 31-32, page 7, lines 5-31, page 8, lines 49-59, Figure 8, abstract).

It is noted that the recitation of "an individual known to be weed pollen allergic" is anticipated by the fact that the diagnostic method of European Patent Application Publication 0 707 065 A2 is directed toward diagnostic procedures for all individuals, which includes those known to be weed pollen allergic. A diagnostic procedure which identifies *Parietaria* allergic individuals from all individuals will inherently identify *Parietaria* allergic individuals from weed pollen allergic individuals.

The claimed invention differs from the prior art in the recitation of "wherein the pure allergen component is Par j 2" in claim 33; and "wherein the pure allergen component is recombinant Par j 2" in claim 36.

Duro et al., teaches contacting serum with recombinant Par j 2 to detect pollen allergy. The reference also teaches that Par j 2 is a new major allergen *of Parietaria judaica* pollen that reacts with the IgE of 82% *of Parietaria judaica* pollen sensitive patients (In particular, abstract, last paragraph, whole document).

It would have been obvious to one of ordinary skill in the art at the time of invention to substitute Par j 2 for Par j 1 in the diagnostic method of European Patent Application Publication 0 707 065 A2 because Duro et al. teaches that Parj 2 is a major allergen *of Parietaria judaica* pollen that reacts with the IgE of 82% of *Parietaria judaica* pollen sensitive patients. One of ordinary skill in the art would have expected a high rate of success from using Par j 2 to diagnose *Parietaria judaica* allergy.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(10) Response to Argument

A. On pages 4-10 of the Appeal Brief, Appellant argues the following:

"The Rejection Under 35 U.S.C. §102(b) Should be Reversed

The methods of claim 30, and claims 31, 32, 34 and 35 dependent on claim 30, are not anticipated by EP '065, whereby the rejection under 35 U.S.C. § 102(b) should be reversed.

More particularly, as defined by claim 30, the invention is directed to a method for serologically identifying with improved accuracy an individual known to be weed pollen allergic as Parietaria allergic, which method comprises selecting an individual known to be weed pollen allergic, wherein it is not known if the individual is Parietaria allergic, and selecting a pure Parietaria allergen component known to have limited or no cross-reactivity. The method further comprises contacting serum from the selected individual known to be weed pollen allergic with the selected pure allergen component, which is pure Par j 1 or Par j 2 allergen component, determining the presence of IgE binding to said pure Par j 1 or Par j 2 allergen component; and identifying the individual as *Parietaria* allergic if the contacted serum contains IgE binding to said pure allergen component.

Thus, the present methods are for accurately identifying a *Parietaria* allergic individual, particularly when the individual is known to be generally weed pollen allergic but it is not known if the individual is *Parietaria* allergic. As described in the present specification, beginning at page 2, line 9, some allergens present in pollen of any particular weed species are represented by structurally similar homologues in other species and therefore show some degree of serological cross-reactivity, whereby sensitization to one weed species may lead to serological test positivity also to other species. Conventional serological testing using pollen extracts will in such cases generate ambiguous results in terms of identification of the actual sensitizer.

Appellants have determined that *Parietaria* pollen extract binds IgE from individuals not exposed to *Parietaria* pollen, while the recited pure allergen component Par j 1 or Par j 2 does not bind to IgE from such individuals. However, Par j 2 does bind IgE from most allergic individuals who are primarily sensitized to *Parietaria* pollen, as does Par j 1. Thus, Appellants have developed the present methods for specific identification of *Parietaria* allergic individuals from those known to be weed pollen allergic using a pure allergen component known to have limited or no cross- reactivity.

Attention is directed to the experimental work described in the present application, beginning at page 3, line 25, wherein the inventors establish that in a test group of patients from Austria (n=42), Scandinavia (n=8), the U.S. (n=lS) and Italy (n=37), almost all patients contained

IgE antibodies to ragweed, mugwort and *Parietaria* pollen extracts (i.e. not pure components). However, only a few Austrian (4) and no Scandinavian or American patients' sera had IgE that bound to Parj 2 (i.e. to the pure component). On the other hand, 81% of the Italian patients contained IgE that bound to Par j 2. Typically, Mediterranean individuals are primarily sensitized to *Parietaria.* Accordingly, the present method is used to determine *Parietaria* allergic individuals.

EP '065 is cited in the Background portion of the present application and discloses recombinant *Parietaria* proteins and derived peptides. Particularly, EP '065 discusses conventional pollen extract immunotherapy and its disadvantages in the lack of standardized extracts, with variations in allergen content and non-allergen protein content (page 2, lines 39-53). EP '065 notes therefore that to eliminate some of the disadvantages of conventional allergenic preparations, research has been conducted to isolate and characterize the individual allergens of the complex repertoire of allergens of a given pollen (page 3, lines 2-4). EP '065 is specifically concerned with the cloning of the major allergens of the genus *Parietaria* (page 2, lines 5-6) and is directed toward the determination of DNA sequences coding for allergenic proteins of *Parietaria* plant pollens (page 3, lines 35-37).

However, EP '065 does not disclose or teach the use of a pure allergen component for accurately identifying a *Parietaria* allergic individual, particularly when the individual is known to be generally weed pollen allergic but it is not known if the individual is *Parietaria* allergic. Importantly, EP '065 does not teach the use of any of the proteins or peptides as reagents to distinguish between genuine *Parietaria* pollen sensitization and cross-reaction-mediated seropositivity to *Parietaria* pollen extract. In fact, in the "Immunoassay" discussion at page 7, lines 5-31, EP '065 discloses that a mixture of peptides may be used either as an immunogen in a composition or as a diagnostic agent, thereby demonstrating the EP '065 does not contemplate the use of a pure *Parietaria* allergen component, particularly a pure *Parietaria* allergen component known to have limited or no cross-reactivity, as compared with mixtures of *Parietaria* allergen components having cross-reactivity, to distinguish between general weed pollen allergy and *Parietaria* allergy.

The Examiner relied on Example 8 of EP '065 as anticipating the claim 30 limitation of "an individual known to be allergic." However, Example 8 does not disclose identification of an individual known to be weed pollen allergic as *Parietaria* allergic according to the limitations of present claim 30 and Example 8 does not indicate that a pure *Parietaria* allergen component known to have limited or no cross-reactivity is employed so that the presence of IgE identifies an individual as *Parietaria* allergic, rather than exhibiting cross-reactivity to one or more *Parietaria* allergens. To the contrary, EP '065 discloses that western blot analysis "of *Parietaria* protein extracts" (page 11, lines 55-56, emphasis added) was conducted. Thus, Example 8 employed extracts, not a pure allergen component. Additionally, El:' '065 discloses that using "pools of sera" (page 11, line 56, emphasis added) from Italy (a pool of 13 sera) and Canada (a pool of 7 sera) showed that a 14 kDa component was recognized by both pools of sera. One of ordinary skill will appreciate that using pooled sera does not provide any diagnostic value relative to an individual. Thus, Example 8 of EP '065 does not anticipate the method of claim 30 of serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria* allergic. At best, Example 8 shows that each of the pools of sera from Italy and Canada contained IgE antibody which reacts with *Parietaria* extract. However, as shown in the

experimental work in the present specification, IgE antibody which reacts with *Parietaria* extract is not determinative of *Parietaria* allergy.

In the final rejection, the Examiner also referenced Example 1 of El:' '065 as anticipating the claimed method as *Parietaria* pollen extracts were separated and purified by SDS PAGE and Western blots were performed using serum from *Parietaria* pollen allergic individuals (page 6 of November 28, 2008 Official Action). However, Example 1 of EP '065 employed "a pool of sera of 7 individuals allergic to *Parietaria* pollen" (page 8, line 57, emphasis added). As in Example 8, one of ordinary skill will appreciate that using pooled sera does not provide any diagnostic value relative to an individual, and El:' '065 provides no teaching or recognition in this regard. Moreover, Example 1 provides no teaching or recognition of the limited or no cross reactivity of any of the separated proteins. One skilled in the art will appreciate that Example 1 of EP '065 is provided to show production and reactivity of murine polyclonal antibodies.

The Examiner asserted in the final rejection that "Knowledge of non-cross reactivity of Par j 1 is not necessary to anticipate the claimed invention" (page 6 of November 28, 2008 Official Action). Appellants respectfully disagree in that claim 30 is directed to serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria* allergic and requires the step of selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity. If a method is conducted without knowledge that the pure allergen component has limited or no cross-reactivity, there could be no identification of the individual as *Parietaria* allergic if the contacted serum contained IgE binding to the pure allergen component, and the limitations of claim 30 are not met.

The Examiner also asserted that it is well known that pooled serum is used for high throughput analysis and pooled serum which demonstrates a positive reaction is further screened (page 7 of November 28, 2008 Official Action). Not only are the Examiner' s assertions completely unsupported by evidence of record, any such techniques are not disclosed by EP '065 which is the basis for the anticipation rejection. Examples 1 and 8 relied upon by the Examiner do not employ serum from a selected individual as recited in claim 30, but instead use pooled sera. Thus, the Examiner's assertions are irrelevant to the present rejection. Moreover, since EP '065 does not disclose that Par j 1, or any other allergen, has limited or no cross reactivity, even if such steps were conducted, there could be no identification of the individual as *Parietaria* allergic if the contacted serum contained IgE binding to the pure allergen component, and the limitations of claim 30 are not met.

The Examiner also asserted that even if the pooled serum could not be used to diagnose allergic individuals, the general teaching of the entire reference is directed to Par j 1 and its use for diagnosis of *Parietaria* pollen allergic individuals (page 7 of November 28, 2008 Official Action). However, the general teachings of EP '065 do not disclose each and every limitation of the method of claim 30, and the Examiner has relied on the specific teachings of Example 8 to assert that the specific limitations of claim 30 are inherent. That specific limitations of claim 30 are not inherent in Example 8 (or Example 1) cannot be ignored in an anticipation rejection by a mere reference to the general teachings of a reference. Further, contrary to the Examiner' s assertion, nowhere does EP '065 specifically disclose a diagnostic method employing only Par j 1 with a serum sample from an individual. To the contrary, EP '065 generally discloses that the recombinant *Parietaria* allergens are useful in diagnosis and therapy of allergic diseases induced by *Parietaria* pollens (Abstract), without any attempt to account for cross reactivity with other pollens.

The Examiner cited *Atlas Powder Company v. IRECO,* 51 U.S.P.Q. 2d 1943 (Fed. Cir. 1999), as supporting the assertion that it is not necessary that those of ordinary skill in the art at the time of the invention knew that Par j 1 had limited or no cross-reactivity. However, the *Atlas Powder* case relates to inherent characteristics or functioning of a prior art composition or ingredient and does not provide any guidance regarding the inherency of a claimed method. Thus, the Atlas Powder case is not relevant to the present anticipation rejection.

Anticipation under 35 U.S.C. § 102 requires that each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference, *In re Robertson,* 49 U.S.P.Q. 2d 1949, 1950 (Fed. Cir. 1999). To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill; inherency may not be established by probabilities or possibilities and the mere fact that a certain thing may result from a given set of circumstances is not sufficient, *In re Robertson,* 49 U.S.P.Q. 2d at 1950- 51. Similarly, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic, *In re Rijckaert,* 28 U.S.P.Q. 2d 1955, 1957 (Fed. Cir. 1993).

EP '065 fails to teach the use of a pure allergen component for serologically identifying an individual, particularly for serologically identifying an individual as *Parietaria* allergic, and EP '065 fails to teach or suggest selecting a pure allergen component known to have limited or no cross-reactivity. While the Examiner has asserted that the steps of the present methods are inherent in the teachings of EP '065, specifically that identifying *Parietaria* allergic individuals from all individuals will inherently identify *Parietaria* allergic individuals from weed pollen individuals, EP '065 does not provide any distinction between for an individual having antibodies binding to *Parietaria* extract versus an individual allergen. Further, the Examiner has not demonstrated any extrinsic evidence which makes clear that the missing elements are necessarily present in the EP '065 teachings, and that the claimed methods would be so recognized by persons of ordinary skill. To the contrary, the teachings of EP '065 relating to the use of a mixture of peptides for diagnostic use (page 7, lines 16-17) and the use of pooled sera (page 8, line 57 and page 11, lines 55-57) contradict the Examiner's assertions regarding inherency as no pure allergen component of known limited or no cross reactivity is employed and no individual is diagnosed using the pooled sera. Thus, EP '065 does not inherently describe the claim elements.

Accordingly, EP '065 does not expressly or inherently disclose each and every element of claim 30. Hence, EP '065 does not anticipate the present claims 30-32, 34 and 35 under 35 U.S.C. § 102, whereby the rejection should be reversed."

Appellant's arguments have been fully considered, but are not found persuasive.

It remains the Examiner's position that European Patent Application Publication 0 707 065 A2 anticipates the claimed invention because the reference specifically teaches the use of purified Par j 1 to diagnose *Parietaria* pollen allergy. Throughout the reference, Par j 1 was

purified and contacted with serum and the reference teaches its use to diagnose *Parietaria* pollen allergy. Knowledge of non- cross-reactivity of Par j 1 is not necessary to anticipate the claimed invention. The reference teaches the use of the same compound to diagnose the same allergy in the same population, therefore the claims are anticipated.

Specifically, European Patent Application Publication 0 707 065 A2 teaches in the last line of the abstract that Par j 1 allergens are "useful in both the diagnosis and therapy of allergic diseases induced by Parientaria pollens." Parietaria judaica is specifically identified as being a weed on page 3, line 23 of the reference. Figure 3 teaches the nucleic acid and amino acid sequences of the Par j 1 allergen variants. On page 4, lines 41-45 the reference teaches "the present invention provides a method of diagnosing an allergic reaction to pollens from Parietaria" using a "diagnostic procedure comprising contacting serum from an individual with the recombinant protein or peptide and pollen specific antibodies in the serum." Immunoassays that may be employed in such a diagnostic method are taught on page 7, lines 5-31.

Figure 1 teaches a Western blot of Parietaria judaica pollen extract that was separated by SDS PAGE and reacted with mouse antiserum to Par j1 or a pool of sera from 7 human individuals known to be allergic to Parietaria pollen (In particular, page 8, line 55 to page 9, line 6). The human serum recognized polypeptide bands that the mouse antiserum specific for Par j1 recognized. Figure 5-6 teaches the generation of overlapping peptides from the Par j 1 allergen and their use as the antigen an ELISA assay that was incubated with pooled serum from five human individuals known to be allergic to Parietaria pollen (In particular, page 10, lines 29-52). Figure 8 teaches the use of Parietaria as the antigen in an ELISA assay that was incubated with pooled serum of 60 human grass allergic individuals and non-grass allergic controls. Figure 9

teaches a Western blot of Parietaria judaica protein extract separated by SDS PAGE and reacted with two pools of sera from individuals from Italy and Canada wherein both pools of serum reacted with the 14 kDa protein corresponding to Par j 1 (In particular, page 11, lines 49-58).

Applicant's recited method does not more accurately identify an individual as being *Parietaria* allergic. The specification discloses on page 1, lines 12-19 that "About 20 % of the western world population suffer from Type I allergy, a hypersensitivity disease involving the formation of IgE antibodies against otherwise harmless molecular structures present in the environment, i.e. allergens. The symptoms of Type I allergy (allergic rhinitis, conjunctivitis and allergic asthma) are mainly caused by the crosslinking of effector-cell bound specific IgE antibodies by allergen molecules, which triggers the release of biological mediators such as histamine and leukotriens that give rise to the tissue reaction." The specification teaches and the art recognizes that when an individual possesses IgE antibodies in their serum against an allergen, the individual is allergic to that allergen. If the antibodies also bind to other allergens due to cross-reactivity, then the individual is allergic to all of the cross-reactive allergens. The specification discloses on page 2, lines 1-6 that allergic cross-reactivity to other allergens may elicit allergic symptoms and be clinically relevant. The information that Par j 1 does not cross react with other allergens that are not in the *Parietaria* species does not distinguish this method over that of the prior art, nor does it more accurately identify an individual as being *Parietaria* allergic. The recited method and that of European Patent Application Publication 0 707 065 A2 are directed to using Par j 1 allergens to diagnose individuals with allergies to *Parietaria*. Applicant's arguments that "Conventional serological testing using pollen extracts will in such cases generate ambiguous results in terms of identification of the actual sensitizer." and that the

prior art does not teach "the use of any of the proteins or peptides as reagents to distinguish between genuine *Parietaria* pollen sensitization and cross-reaction-mediated seropositivity to *Parietaria* pollen extract." are directed to limitations that are not present in the claims. The claims are not directed to determining the actual sensitizer or original allergen source responsible for triggering the allergic reaction. The claims are directed to determining if is an individual is *Parietaria* allergic and they are if they have IgE antibodies that bind to Par j 1.

Applicant's arguments with respect to knowledge of cross-reactivity are not persuasive for the reason argued *supra*. In addition, the step of selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity does not lend patentable weight to the claims. The method is directed to using the exact same purified allergens to diagnose the exact same allergy. The knowledge that the pure allergen component has limited or no cross-reactivity does not lend patentable weight to the claims. The Examiner's citation of Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) does provide guidance regarding the inherency of a claimed method and is relevant to the present anticipation rejection. Applicant is attempting to rely on a previously unappreciated property of the allergen used in the method in order to make the method patentably distinct. Cross-reactivity is an intrinsic property of the Par j 1 allergen. See In re Cruciferous Sprout Litigation, 301 F.3d 1343, 64 USPQ2d 1202 (Fed. Cir. 2002). There are no active steps that make the method any different than that of the prior art. The method performed with or without the knowledge of cross-reactivity still results in the determination of whether or not an individual has IgE antibodies that bind Par j 1 wherein the presence of IgE binding to Par j 1 indicates that the individual is *Parietaria* allergic.

Furthermore, Applicant's argument that one of ordinary skill will appreciate that using pooled sera does not provide any diagnostic value relative to an individual is also unpersuasive. First, the diagnostic method is taught generally in the reference, so there is no requirement that the use of pooled serum samples in the reference provide the only support for the recited method. Second, the diagnostic method may be performed using pooled serum of individuals who are weed pollen allergic, but not Parietaria allergic and it would provide diagnostic value to all individuals in pooled serum. Negative results still meet the claim limitations.

In conclusion, the rejection should be maintained for the reasons cited supra. European Patent Application Publication 0 707 065 A2 teaches a method for identifing an individual as Parietaria allergic comprising contacting serum from the individual with recombinant Par j 1, determining the presence of IgE binding to Par j 1 and identifying the individual as Parietaria allergic if the serum contains IgE binding to Par j 1. The method teaches performing the method in all individuals, which includes those known to be weed pollen allergic. The knowledge of Par j1 having limited or no cross-reactivity does not improve the accuracy of the method, nor does it lend patentable weight because it is not an active step.

B. On pages 11-15 of the Appeal Brief, Appellant argues the following:

> "The Rejection Under 35 U.S.C. §103(a) Should be Reversed
>
> The methods of claim 30, and claims 33, 34 and 36 dependent on claim 30, are nonobvious over and patentably distinguishable from the combination of EP '065 and Duro et al, whereby the rejection under 35 U.S.C. § 103(a) should be reversed.

The method of claim 30, as well as the deficiencies of EP '065 with respect to the method of claim 30 are discussed in detail above and are incorporated herein in traversing the rejection under 35 U.S.C. § 103(a). That is, EP '065 does not disclose or teach the use of a pure allergen component for accurately identifying a Parietaria allergic individual, particularly when the individual is known to be generally weed pollen allergic but it is not known if the individual is Parietaria allergic. Importantly, EP '065 does not teach the use of any of the proteins or peptides as reagents to distinguish between genuine Parietaria pollen sensitization and cross-reaction-mediated seropositivity to Parietaria pollen extract. In fact, in the "Immunoassay" discussion at page 7, lines 5-31, EP '065 discloses that a mixture of peptides may be used either as an immunogen in a composition or as a diagnostic agent, thereby demonstrating the EP '065 does not contemplate the use of a pure *Parietaria* allergen component, particularly a pure *Parietaria* allergen component known to have limited or no cross-reactivity, as compared with mixtures of *Parietaria* allergen components having cross-reactivity, to distinguish between general weed pollen allergy and *Parietaria* allergy.

The deficiencies of EP '065 are not resolved by Duro et al in that Duro et al similarly fail to teach a method for serologically identifying an individual known to be weed pollen allergic wherein it is not known if the individual is *Parietaria* allergic. That is, Duro et al are directed to a single allergen source, namely *Parietaria judaica* pollen, and do not mention other allergen sources or individuals known generally to be weed pollen allergic. While Duro et al seek to characterize one of at least 9 allergen components of this source, namely Par j 2, Duro et al are not concerned with any other allergy source. Further, by showing that 82% of the *Parietaria judaica* pollen sensitive patients' serum had IgE reacting with Parj 2, Duro et al merely show that Parj 2 is a major allergen (see page 297, right column, lines 18-21), and no other findings or conclusions are provided by Duro et al. Particularly, Duro et al do not teach or suggest that Par j 2, or any other pure allergen component, has limited or no cross reactivity and therefore can be employed in order to serologically identify with improved accuracy a *Parietaria* allergic individual from a general weed pollen allergic individual, as recited in present claim 30. In fact, while claim 30 recites the step of selecting an individual known to be weed pollen allergic, wherein it is not known if the individual is *Parietaria* allergic, Duro et al employ serum from individuals assertedly known to be *Parietaria* allergic. Further, while claim 30 requires selecting a pure *Parietaria* allergic component known to have limited or no cross-reactivity, Duro et al fail to teach, suggest or recognize that Par j 2 has limited or no cross-reactivity.

Importantly, Duro et al provide no teaching or suggestion that Par j 2 is a known pure allergen component with limited or no cross-reactivity. The previously submitted Declaration Under 37 C.F.R. 1.132 of the co-inventor Dr. Paolo Colombo confirms that the Duro et al paper does not disclose or suggest that the Par j 2 allergen has limited or no cross-reactivity with allergen components from other weed pollen allergen sources (paragraph 4) and thus does not teach or suggest using Par j 2, or any other purified allergen component, in methods for diagnosis of the actual sensitizing source from a variety of possible allergen sources (paragraph 4).

As in the anticipation rejection, the Examiner again asserted that whether or not individuals in the prior art were knowingly being serologically identified as *Parietaria* allergic is not necessary as the method is inherently identifying them (page 13 of November 28, 2008 Official Action). However, claim 30 is specifically directed to a method for identifying such an individual and particularly so identifying such an individual when the individual is known to be weed pollen allergic. If the prior art does not recognize the individual as identified as *Parietaria* allergic, as distinguished from weed pollen allergic, the prior art does not teach the claimed

method. Moreover, as discussed in detail above, EP '065 teaches the use of pooled sera and therefore even if the Par j 2 of Duro et al were employed in place of Parj 1 in Examples 1 and/or 8 of EP '065, a method as recited in claim 30 would simply not result as no individual is identified.

Further, the Examiner asserted that Applicants' own specification and responses evidence that the *Parietaria* allergic individuals whose serum did not bind Par j 2 must inherently not be *Parietaria* allergic at all (page 13 of November 28, 2008 Official Action). However, the teachings of Applicants' specification and the descriptions of Applicants' invention in prosecution responses are not available as prior art to interpret what the Duro et al teachings would mean to one of ordinary skill in the art. As Duro et al still identify the individuals whose serum did not bind Par j 2 as *Parietaria* allergic, it is clear that Duro et al do not recognize or suggest the use of Par j 2 in a method as recited in claim 30 for identifying *Parietaria* allergic individuals from weed pollen allergic individuals. To the contrary, Duro et al teach away from the presently claimed method in still identifying the individuals whose serum did not bind Par j 2 as *Parietaria* allergic. Hence, Duro et al do not resolve the deficiencies of EP '065.

Only in light of Applicants' specification can the Examiner conclude that the 18% of patients having serum which did not react with Par j 2 are inherently not allergic to *Parietaria judaica* and therefore must be allergic to another allergen from another weed pollen source while the 82% of patients having serum that reacts with Par j 2 are *Parietaria* allergic. Contrary to the Examiner's assertion that EP '065 and Duro et al need not teach or recognize that Par j 2 is of limited or no cross-reactivity, the step of selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity of claim 30 requires that EP '065 or Duro et al must provide this very teaching in order to anticipate the claimed method for serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria* allergic.

All words in a claim must be considered in judging the patentability of the claim against the prior art, *In re Wilson,* 424 F.2d 1382, 1385 (CCPA 1970); MPEP 2143.03. In the present rejection, the Examiner has improperly disregarded several limitations of the method of claim 30 to conclude that the combination of EP '065 and Duro et al render claim 30 obvious. For example, in relying on EP '065's Examples 1 and 8 employing pooled sera, the Examiner has improperly disregarded the fact that an individual is identified in the method of claim 30 and has disregarded that fact that serum from the individual is contacted with the pure allergen component in the method of claim 30 to make the individual identification. Further, in concluding that it is not necessary to know the limited or no cross reactivity of Parj 1 or Parj 2, the Examiner has improperly disregarded the fact that claim 30 recites the step of selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity, and has improperly disregarded that fact that the known limited or no cross-reactivity is necessary to make the identification required in the final step of claim 30. Accordingly, all words in claim 30 have not been considered in judging the patentability of claim 30.

As a result, the Examiner has not properly evaluated all of the differences between the invention as defined by claim 30 and the prior art of EP '065 and Duro et al as required by *Graham v. John Deere Co.,* 383 U.S. 1 (1966). Once the differences noted above are properly recognized, it is evident that the combination of EP '065 and Duro et al fails to render obvious a method for serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria* allergic, particularly an individual known to be weed pollen allergic, wherein it is not known if the individual is *Parietaria* allergic as recited in claim 30. Accordingly,

EP '065 in view of Duro et al does not render present claims 30, 33, 34 and 36 obvious under 35 U.S.C. § 103, whereby the rejection should be reversed."

Appellant's arguments have been fully considered, but are not found persuasive.

It remains the Examiner's position that European Patent Application Publication 0 707 065 A2 specifically teaches the use of purified Par j 1 to diagnose *Parietaria* pollen allergy. Throughout the reference, Par j 1 was purified and contacted with serum and the reference teaches its use to diagnose *Parietaria* pollen allergy. Knowledge of non- cross-reactivity of Par j 1 is not necessary.

Specifically, European Patent Application Publication 0 707 065 A2 teaches in the last line of the abstract that Par j 1 allergens are "useful in both the diagnosis and therapy of allergic diseases induced by Parientaria pollens." Parietaria judaica is specifically identified as being a weed on page 3, line 23 of the reference. Figure 3 teaches the nucleic acid and amino acid sequences of the Par j 1 allergen variants. On page 4, lines 41-45 the reference teaches "the present invention provides a method of diagnosing an allergic reaction to pollens from Parietaria" using a "diagnostic procedure comprising contacting serum from an individual with the recombinant protein or peptide and pollen specific antibodies in the serum." Immunoassays that may be employed in such a diagnostic method are taught on page 7, lines 5-31.

Figure 1 teaches a Western blot of Parietaria judaica pollen extract that was separated by SDS PAGE and reacted with mouse antiserum to Par j 1 or a pool of sera from 7 human individuals known to be allergic to Parietaria pollen (In particular, page 8, line 55 to page 9, line 6). The human serum recognized polypeptide bands that the mouse antiserum specific for Par j1

recognized. Figure 5-6 teaches the generation of overlapping peptides from the Par j 1 allergen and their use as the antigen an ELISA assay that was incubated with pooled serum from five human individuals known to be allergic to Parietaria pollen (In particular, page 10, lines 29-52). Figure 8 teaches the use of Parietaria as the antigen in an ELISA assay that was incubated with pooled serum of 60 human grass allergic individuals and non-grass allergic controls. Figure 9 teaches a Western blot of Parietaria judaica protein extract separated by SDS PAGE and reacted with two pools of sera from individuals from Italy and Canada wherein both pools of serum reacted with the 14 kDa protein corresponding to Par j 1 (In particular, page 11, lines 49-58).

It remains the Examiner's position that Duro et al. is being relied on for its teaching that Parj 2 is a major allergen that can be used to distinguish individuals based upon their IgE binding profile. Duro et al. teaches contacting serum with recombinant new major allergen Par j 2 *of Parietaria judaica* pollen to detect pollen allergy that reacts with the IgE of 82% *of Parietaria judaica* pollen sensitive patients. It would have been obvious to one of ordinary skill in the art at the time of invention to substitute Par j 2 for Par j 1 in the diagnostic method of European Patent Application Publication 0 707 065 A2 because Duro et al. teaches that Par j 2 is a major allergen *of Parietaria judaica* pollen that reacts with the IgE of 82% *of Parietaria judaica* pollen sensitive patients.

Applicant's recited method does not more accurately identify an individual as being *Parietaria* allergic. The specification discloses on page 1, lines 12-19 that "About 20 % of the western world population suffer from Type I allergy, a hypersensitivity disease involving the formation of IgE antibodies against otherwise harmless molecular structures present in the environment, i.e. allergens. The symptoms of Type I allergy (allergic rhinitis, conjunctivitis and

allergic asthma) are mainly caused by the crosslinking of effector-cell bound specific IgE antibodies by allergen molecules, which triggers the release of biological mediators such as histamine and leukotriens that give rise to the tissue reaction." The specification teaches and the art recognizes that when an individual possesses IgE antibodies in their serum against an allergen, the individual is allergic to that allergen. If the antibodies also bind to other allergens due to cross-reactivity, then the individual is allergic to all of the cross-reactive allergens. The specification discloses on page 2, lines 1-6 that allergic cross-reactivity to other allergens may elicit allergic symptoms and be clinically relevant. The information that Par j 1 and Par j 2 do not cross react with other allergens that are not in *Parietaria* species does not distinguish this method over that of the prior art, nor does it more accurately identify an individual as being *Parietaria* allergic. The recited method and that of European Patent Application Publication 0 707 065 A2 are directed to using Par j 1 allergens to diagnose individuals with allergies to *Parietaria*. Applicant's arguments that "Conventional serological testing using pollen extracts will in such cases generate ambiguous results in terms of identification of the actual sensitizer." and that the prior art does not teach "the use of any of the proteins or peptides as reagents to distinguish between genuine *Parietaria* pollen sensitization and cross-reaction-mediated seropositivity to *Parietaria* pollen extract." are directed to limitations that are not present in the claims. The claims are not directed to determining the actual sensitizer or original allergen source responsible for triggering the allergic reaction. The claims are directed to determining if is an individual is *Parietaria* allergic and they are if they have IgE antibodies that bind to Par j 1 or Par j 2.

Applicant's arguments with respect to knowledge of cross-reactivity are not persuasive for the reason argued *supra*. In addition, the step of selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity does not lend patentable weight to the claims. The method is directed to using the exact same purified allergens to diagnose the exact same allergy. The knowledge that the pure allergen component has limited or no cross-reactivity does not lend patentable weight to the claims. The Examiner's citation of See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) does provide guidance regarding the inherency of a claimed method and is relevant to the present anticipation rejection. Applicant is attempting to rely on a previously unappreciated property of the allergen used in the method in order to make the method patentably distinct. Cross-reactivity is an intrinsic property of the Par j 1 and Par j 2 allergens. See In re Cruciferous Sprout Litigation, 301 F.3d 1343, 64 USPQ2d 1202 (Fed. Cir. 2002). There are no active steps that make the method any different than that of the prior art. The method performed with or without the knowledge of cross-reactivity still results in the determination of whether or not an individual has IgE antibodies that bind Par j 1 or Par j 2 wherein the presence of IgE binding to Par j 1 or Par j2 indicates that the individual is *Parietaria* allergic.

Furthermore, Applicant's argument that one of ordinary skill will appreciate that using pooled sera does not provide any diagnostic value relative to an individual is also unpersuasive. First, the diagnostic method is taught generally in the European Patent Application Publication 0 707 065 A2 reference, so there is no requirement that the use of pooled serum samples in the reference provide the only support for the recited method. Second, the diagnostic method may be performed using pooled serum of individuals who are weed pollen allergic, but not Parietaria

allergic and it would provide diagnostic value to all individuals in pooled serum. Negative results still meet the claim limitations.

In conclusion, the rejection should be maintained for the reasons cited supra. European Patent Application Publication 0 707 065 A2 teaches a method for identifing an individual as Parietaria allergic comprising contacting serum from the individual with recombinant Par j 1, determining the presence of IgE binding to Par j 1 and identifying the individual as Parietaria allergic if the serum contains IgE binding to Par j 1. The method teaches performing the method in all individuals, which includes those known to be weed pollen allergic. The knowledge of Par j1 having limited or no cross-reactivity does not improve the accuracy of the method, nor does it lend patentable weight because it is not an active step. It would have been obvious to one of ordinary skill in the art at the time of invention to substitute Par j 2 for Par j 1 in the diagnostic method of European Patent Application Publication 0 707 065 A2 because Duro et al. teaches that Par j 2 is a major allergen *of Parietaria judaica* pollen that reacts with the IgE of 82% *of Parietaria judaica* pollen sensitive patients.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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